

### REMARKS

Claims 1-17 are currently pending in this application. Claims 1-17 have been examined and stand rejected on arguments laid out in the Non-Final Office Action mailed on January 24, 2007. Applicant thanks the Examiner for the careful examination of this case, and respectfully requests reexamination and reconsideration of the case, as amended.

The present Amendment amends claims 1, 9, 12, 14, and 15; and cancels claims 7, 8, and 13. No new matter is added to this case by the present Amendment. Applicant is submitting the present Amendment without prejudice to the subsequent prosecution of claims to some or all of the subject matter which might be lost by virtue of this paper, and explicitly reserves the right to pursue some or all of such subject matter, in Divisional or Continuation Applications.

Below Applicant addresses each of the rejections levied in the Office Action and explains why the rejections are not applicable to the pending claims.

#### Amendments to the Specification

As requested by the Examiner, the first paragraph following “Related Applications” has been amended to include reference to the International Application from which the instant application is a national stage entry.

As requested by the Examiner, trademarks have been capitalized throughout the specification.

#### Amendments to the Claims and Support for Amendment

Independent claim 1 has been amended to replace the phrase “*in combination with*” by its definition, as it appears in the application, as originally filed (see, for example, the second paragraph on page 24 of the application). As amended, claim 1 recites “*a method for treating cancer comprising administering chlorotoxin or a chlorotoxin derivative as a first agent and at least one chemotherapeutic agent as a second agent, wherein the two agents are administered simultaneously or are administered independently in a fashion that the agents will act at the same time, wherein....*”

Claims 1, 9 and 14 have been amended to introduce a limitation regarding the chlorotoxin derivative. As amended, claims 1, 9 and 14 contain the following limitation: “*wherein the chlorotoxin derivative comprises a sequence selected from the group consisting of SEQ ID No. 1, SEQ ID No. 2, SEQ ID No. 3, SEQ ID No. 4, SEQ ID No. 5, SEQ ID No. 6, SEQ ID No. 7, SEQ ID No. 8, SEQ ID No. 13, portions thereof, and combinations thereof.*” Support for this amendment can be found, for example, at lines 25-32 of page 10 of the application, as originally filed, and in the paragraph starting on page 11 and ending on page 12 of the application, as originally filed.

Claims 1, 12, and 15 have been amended to introduce a limitation regarding the cancer to be treated. As amended, claims 1, 12 and 15 read “*wherein the cancer is a member of the group consisting of human glioblastoma multiforme, human malignant melanoma, human prostate tumor, and human small cell lung carcinoma.*” Support for this amendment can be found throughout the specification, for example, in the Examples section.

#### Claim Objection

Claim 4 is objected to under 37 CFR § 1.75 as being a substantial duplicate of claim 1. Claim 1, as originally filed, reads “*a method for treating cancer comprising administering chlorotoxin or a chlorotoxin derivative in combination with at least one chemotherapeutic agent*”. Claim 4, as originally filed, reads “*a method according to claim 1 wherein chlorotoxin or a chlorotoxin derivative is administered simultaneously with the chemotherapeutic agent*”.

Applicant respectfully disagrees with the Examiner’s objection and points out that the term “in combination” is explicitly defined in the Specification. For example, the second paragraph on page 24 of the application as originally filed, contains the following sentence: “*As used herein, two agents are said to be administered in combination when the two agents are administered simultaneously or are administered independently in a fashion that the agents will act at the same time.*” Thus, claim 4 is not a substantial duplicate of claim 1, as originally filed; the objection should be removed. Applicant further submits that claim 4 is also not a substantial duplicate of claim 1, as amended, which specifically recites the definition of the term “in combination with”.

#### Claim Rejections – 35 U.S.C. § 112

Claims 1-8 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner has rejected claims 1-3 as being indefinite and stated that the meaning of the phrase “in combination” is unclear in claim 1.

As already mentioned above, the term “*in combination with*” is explicitly defined in the Specification of the application as originally filed, and claim 1 has been amended to recite this definition.

Claims 1-17 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which is not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular, the Examiner states that the claims are drawn to a genus, *i.e.*, chlorotoxin derivatives, which is defined in the specification to be synonymous with variant. The Examiner has taken the position that one of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus of which comprises all chlorotoxin derivatives as defined broadly.

Applicant respectfully disagrees and submits that the rejection is irrelevant to the claims, as amended. In particular, Applicant points out that a limitation regarding the chlorotoxin derivative has been introduced to independent claims 1, 9 and 14, which specifies that the chlorotoxin derivative comprises a sequence selected from the group consisting of SEQ ID No. 1, SEQ ID No. 2, SEQ ID No. 3, SEQ ID No. 4, SEQ ID No. 5, SEQ ID No. 6, SEQ ID No. 7, SEQ ID No. 8, SEQ ID No. 13, portions thereof, and combinations thereof. Therefore, the rejection does not apply to the claims, as amended.

Claims 1-17 stand rejected under 35 U.S.C. § 112, first paragraph. In particular, the Examiner states that the specification, while being enabling for methods of treating and detecting human glioblastoma multiforme, human malignant melanoma, human prostate cancer and human small cell lung carcinoma does not reasonably provide enablement for all other cancers as instantly claimed. The Examiner has taken the position that the specification does not enable a

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant respectfully disagrees and submits that the rejection is irrelevant to the claims, as amended. In particular, Applicant points out that a limitation has been introduced to claims 1, 12 and 15, which specifies that the cancer is a member of the group consisting of human glioblastoma multiforme, human malignant melanoma, human prostate tumor, and human small cell lung carcinoma. Therefore, the rejection does not apply to the claims, as amended, and should be removed.

#### Claim Rejections – 35 U.S.C. § 102

Claims 14-17 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Soroceanu *et al.* (Cancer Research, Nov. 1, 1998, 58: 4871-4879). The Examiner states that Soroceanu *et al.* teaches the use of chlorotoxin (CTX) for targeting tumors (*e.g.*, brain tumors) with radiolabeled CTX, for example, labeled with <sup>125</sup>I and <sup>131</sup>I.

Applicants respectfully disagrees and points out that independent claim 14 has been amended to delete the term “labeled chlorotoxin”. As amended, claim 14 recites: “a method for detecting the presence of cancer in a patient comprising administering a detectable amount of labeled chlorotoxin derivative, ...”. The rejection is moot.

Claims 14-17 stand rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Pat. No. 6,667,156 (‘156). The Examiner has taken that position that ‘156 teaches the use of radiolabeled chlorotoxin (CTX) for targeting tumors (brain tumors, gliomas, meningiomas, ependymomas, medulloblastomas, neuroblastomas, glioblastomas, gangliomas, melanoma, sarcoma, pheochromocytoma, small cell lung carcinoma, and metastatic brain tumors) for example, chlorotoxin labeled with <sup>3</sup>H, <sup>14</sup>C, <sup>32</sup>P, <sup>35</sup>S, <sup>36</sup>CR, <sup>57</sup>Co, <sup>59</sup>Fe, <sup>90</sup>Y, <sup>186</sup>Re, <sup>125</sup>I, or <sup>131</sup>I.

As mentioned above, the term “labeled chlorotoxin” has been deleted from independent claim 14. The rejection does not apply to the claims, as amended.

#### Claim Rejections – 35 U.S.C. § 103

Claims 1-17 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Pre-Grant Publication No. 2002-0146749 (‘6749), which was filed on January 22, 2001, in

combination with U.S. Pre-Grant Publication No. 2001-0055751 ('5751), which was filed on May 3, 2000.

The Examiner states that '6749 teaches the use of radiolabeled (*e.g.*, radiolabeled with  $^3\text{H}$ ,  $^{14}\text{C}$ ,  $^{32}\text{P}$ ,  $^{35}\text{S}$ ,  $^{36}\text{Cl}$ ,  $^{57}\text{Co}$ ,  $^{59}\text{Fe}$ ,  $^{90}\text{Y}$ ,  $^{186}\text{Re}$ ,  $^{125}\text{I}$ , and  $^{131}\text{I}$ ) chlorotoxin (CTX) for targeting tumors (brain tumors, gliomas, meningiomas, ependymomas, medulloblastomas, neuroblastomas, glioblastomas, gangliomas, pheochromocytoma, melanoma, sarcoma, small cell lung carcinoma, and metastatic brain tumors). The Examiner also states that '6749 further teaches compositions and treatment of cancers by administration of chlorotoxin in combination with cytotoxic moieties of gelonin, ricin, saponin, pseudomonas exotoxin, pokeweed antiviral protein, and diphtheria toxin. The Examiner admits, however, that '6749 does not teach those chemotherapeutics claimed in the instant application. The Examiner further states that '5751 teaches prostate carcinoma treatments comprising the use of immunoconjugates with cytotoxic agents such as ricin, doxorubicin, daunorubicin, mitomycin, etoposide, teniposide, vincristine, diphtheria toxin, pseudomonas exotoxin, and gelonin; and acknowledges that '5751 does not teach the use of chlorotoxin in the compositions or their uses.

The Examiner has taken the position that it would have been obvious to combine the cytotoxic/chemotherapeutic agents taught in overlap by the two references for the genus of cancers taught in the two references that are instantly claimed, and one of ordinary skill in the art would have a high expectation of success in using those obvious compounds for treatment of those cancers.

Applicants submit that '6749 teaches the use of a ligand specific for tumors of neuroectodermal origin (*e.g.*, chlorotoxin or an antibody against the chlorotoxin receptor) fused to a cytotoxic moiety (*e.g.*, gelonin, ricin, saponin, pseudomonas exotoxin, pokeweed antiviral protein, diphtheria toxin, and complement proteins) for targeting/treating tumors (see, for example, paragraphs [0020]-[0022] of publication '6749). Thus, in compositions and methods described in '6749, chlorotoxin is covalently linked to the cytotoxic moiety, and the specificity of chlorotoxin for tumors of neuroectodermal origin is used for targeting the cytotoxic moiety to this type of neoplastic tissues.

Applicant further submits that '5751 teaches prostate carcinoma treatments comprising the use of antibodies that specifically bind to PSMA on the surface of carcinoma cells, wherein

the antibodies are conjugated to therapeutic agents (e.g., cytotoxic agents such as ricin, doxorubicin, daunorubicin, mitomycin, etoposide, teniposide, vincristine, diphtheria toxin, pseudomonas exotoxin, and gelonin). Thus, treatment methods described in '5751 involve administration of immunoconjugates, i.e., antibodies covalently linked to therapeutic agents (see, for example, paragraph [0143] of publication '5751). In these treatment methods, the immunoconjugate is used for targeting the therapeutic agent to a PSCA positive cell (see paragraph [0144] of publication '5751).

Thus, both the '6749 reference and '5751 reference describe a method for the treatment of a cancer or cancers involving administration of a targeting moiety covalently linked to a therapeutic agent (e.g., a cytotoxic agent), wherein the targeting moiety exhibits high affinity/specificity for tissue or cells of the cancer or cancers. Since both references describe the use of a conjugate (i.e., a single agent), any combination of the references can only teach the use of a conjugate (i.e., a single agent). Neither '6749 nor '5751 teaches or suggests administration of chlorotoxin, or a chlorotoxin derivative, as a first agent and at least one chemotherapeutic agent as a second agent to treat cancer. Similarly, neither '6749 nor '5751 teaches or suggests compositions comprising chlorotoxin, or a chlorotoxin derivative, and at least one chemotherapeutic agent, as recited in the instant claims. Furthermore, combining the teaching of '6749 and '5751 would not lead one of ordinary skill in the art to the instant invention where chlorotoxin, or a chlorotoxin derivative, and a chemotherapeutic agent (i.e., two agents which are not covalently linked to each other) are administered in combination (i.e., simultaneously or independently in a fashion that they will act at the same time) to treat cancer.

For the reasons set forth above, Applicant submits that '6749 and '5751 (taken alone or in combination) do not anticipate the currently pending claims, and respectfully requests that the rejection be withdrawn.

### CONCLUSION

Applicant again thanks the Examiner for the careful review of the case. The claims have been amended to obviate all rejections. Based on the Remarks presented above, Applicant respectfully submits that Claims 1-6, 9-12, and 14-17 are now in condition for allowance. A Notice to this effect is respectfully requested.

Please charge any fees that may be associated with this matter, or credit any overpayments, to our Deposit Account No.: 03-1721.

Respectfully submitted,

/BHJarrell/

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